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HELLP syndrome as a major contributor to adverse maternal and neonatal outcomes among preeclamptic women: findings from a multicenter retrospective cohort study

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Abstract

Objective HELLP syndrome, a severe complication of preeclampsia, is associated with increased maternal and neonatal morbidity and mortality. This study aims to evaluate maternal and perinatal outcomes in preeclamptic women with and without HELLP syndrome in Indonesia.

Methods A multicenter retrospective cohort study was conducted across 30 hospitals in Indonesia from January 2022 to December 2023. Data from 1,808 preeclamptic women were analyzed, with 219 (12.1%) classified as having HELLP syndrome. Maternal and perinatal outcomes were compared between the HELLP and non-HELLP groups.

Results Women with HELLP syndrome had significantly higher risks of severe complications, including eclampsia ($p < 0.001$; aOR: 2.5 (1.5–4.18)), acute kidney injury ($p < 0.01$; aOR: 4.11 (2.07–8.15)), emergency hypertension ($p = 0.048$; aOR: 1.42 (1.01–2.01)), preterm birth < 37 weeks ($p = 0.013$; aOR: 1.54 (1.1–2.17)), and preterm birth < 34 weeks ($p < 0.001$; aOR: 1.8 (1.28–2.53)). HELLP syndrome increased the risk of Intra-uterine fetal death ($p = 0.01$; aOR: 2.18 (1.21–3.95)) and neonatal sepsis ($p = 0.011$; aOR: 2.32 (1.21–4.42)). Although the multivariate analysis did not yield any significant results, the HELLP syndrome group has a substantially higher prevalence of maternal death (3.7% vs 1%; $p = 0.005$) and neonatal death (11.6% vs 6.4%; $p = 0.005$).

Conclusion HELLP syndrome significantly worsens maternal and neonatal outcomes in preeclampsia, reflecting a need for improved early detection of 'high-risk' preeclamptic women like sFlt1/PLGF ratio and perhaps other laboratory tests like haptoglobin and D-dimer's. Many of these laboratory tests are currently not accessible in the Indonesian public health sector. Further research is needed to identify other markers that would assist in a more timely diagnosis of impending HELLP syndrome, particularly in early-onset preeclampsia patients managed conservatively.

Keywords HELLP syndrome, Preeclampsia, Maternal mortality, Perinatal outcomes, Pregnancy complications

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Background

HELLP syndrome, which stands for Hemolysis, Elevated Liver enzymes, and Low Platelet count, is a severe and potentially life-threatening complication that can occur during pregnancy or shortly after childbirth. The HELLP acronym was first introduced by Weinstein in 1982. HELLP syndrome is characterized by the breakdown of red blood cells (hemolysis), elevated liver enzymes, and a low platelet count, which can lead to various maternal and fetal complications [1, 2]. The incidence of HELLP syndrome worldwide is estimated to range from 0.5% to 0.9% of all pregnancies, and it is considered a variant of preeclampsia (PE) [3]. Regrettably, there is no formal documentation concerning the occurrence of HELLP syndrome in South Asia, particularly in Indonesia. In our articles of all preeclampsia cases from 11 tertiary referral centers in Indonesia (2016), the incidence of HELLP syndrome was 9.8% [4].

HELLP syndrome is a serious condition that can have significant implications for both the mother and the developing fetus. HELLP syndrome increase the risk of maternal complications such as eclampsia, cerebral hemorrhage, liver rupture, and acute respiratory distress syndrome [5–7]. Moreover, HELLP syndrome is a leading cause of iatrogenic preterm birth, which in turn can result in increased infant mortality and morbidity [8]. The risk of maternal and perinatal death with the presence of HELLP syndrome is significantly higher compared to preeclamptic pregnancies without HELLP syndrome. This is supported by the result of studies which found that the perinatal mortality rate in women with HELLP syndrome was 25% as compared to 3.7% in those without HELLP syndrome [9, 10]. Maternal mortality results from complications including pulmonary edema, renal failure, disseminated intravascular coagulation, and subcapsular liver hematoma [11]. Perinatal mortality is predominantly associated with gestational age at birth or preterm [12]. There are limited data about the pregnancy outcomes associated with HELLP syndrome in PE women, especially in developing countries. The aim of this study is to explore the maternal and perinatal outcomes associated with HELLP syndrome in a cohort of women with preeclampsia in Indonesia.

Methods

Study design, sampling, and recruitment

This is a multicenter observational retrospective cohort study part of The INAPRES study (Indonesia Preeclampsia Study) carried out in Indonesia [13]. This research was orchestrated and conducted by the Himpunan Kedokteran Fetomaternal Indonesia (*Indonesian Maternal Fetal Medicine Association*). Data were collected from 30 hospitals across 5 major islands in Indonesia between January 2022 and December 2023. Data collecting sites

were categorized by regions: Java Island (17 hospitals), Sumatra Island (7 hospitals), Kalimantan (2 hospitals), Sulawesi (2 hospitals), and Bali—West Nusa Tenggara (2 hospitals). Data were obtained from medical records using both manual and electronic approaches. The ethics council of Airlangga University Hospital has issued ethical approval for this research (approval no. 052/KEP/2024, protocol number UA-02–24074). This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments. The Ethics Committee of Airlangga University Hospital has waived the requirement for informed permission to participate, owing to the retrospective study design (all data were sourced from medical records). The inclusion criteria encompass all pregnancies affected by PE that resulted in delivery at the hospital where the trial was conducted between January 2022 and December 2023. Exclusion criteria were applied exclusively when pregnancy outcome data were insufficiently documented in medical records. The sample size represents the total sampling conducted throughout the study period, adjusted based on the inclusion and exclusion criteria. The sample was later categorized into two groups depending on the presence of HELLP syndrome: the HELLP syndrome group and the PE non-HELLP group.

Primary outcomes

This study's principal outcomes included essential risk factors, maternal outcomes, complications during labor, and perinatal outcomes associated with HELLP syndrome. Maternal outcomes encompassed severe PE, eclampsia, pulmonary edema, acute renal failure, emergency hypertension, cerebrovascular accident (CVA), preterm birth (prior to 34 and 37 weeks), fetal growth restriction (FGR), intrauterine fetal demise (IUFD), blood pressure, intensive care unit (ICU) admission, delivery method, and postpartum hemorrhage. Labour difficulties are defined as any occurrences that occur during or subsequent to delivery. It comprised eclampsia, cerebrovascular accident (CVA), hypovolemic shock (PPH), uterine atony, perineal rupture, cervical rupture, and an extended second stage of labor. Perinatal outcomes encompassed: birth weight, birth length, Apgar scores at the 1st and 5th minutes, NICU admission, neonatal mortality, and newborn morbidity (sepsis, RDS, NEC, ICH) and IUFD.

Definition

HELLP syndrome is identified by the following criteria: lactate dehydrogenase (LDH) levels up to 600 IU/L or greater, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels exceeding twice the upper limit of normal, and a platelet count below $100 \times 10^9/L$. PE is diagnosed based on the ISSHP criteria, necessitating the presence of pregnancy hypertension accompanied

by one of the following symptoms occurring after 20 weeks of gestation: proteinuria, maternal end-organ failure, or uteroplacental dysfunction [14]. Severe PE is diagnosed in accordance with ACOG guidelines, specifically through the identification of one or more of the following symptoms: blood pressure surpassing 160/110 mmHg, thrombocytopenia, impaired liver function (elevated liver enzymes exceeding twice the upper limit of normal), epigastric pain, renal impairment (serum creatinine levels exceeding twice the normal limit), pulmonary edema, severe headache, or visual disturbances. Eclampsia is defined by the occurrence of tonic-clonic, focal, or multifocal seizures in the absence of other etiologies, such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or substance abuse (ACOG definition) [15]. Emergency hypertension in PE is characterized by a systolic blood pressure (SBP) of 160 mm Hg or more, or a diastolic blood pressure (DBP) of 110 mm Hg or

more. The diagnosis of cerebrovascular accident (CVA) relies on the manifestation of acute neurological symptoms, including headache, weakness, visual disturbances, and seizures, and is substantiated through imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI). Fetal Growth Restriction (FGR) is diagnosed when fetal weight is below the 10th percentile for gestational age by antenatal ultrasound.

Data analysis

Data analysis and statistical assessment were performed utilizing SPSS version 29. Categorical data will be quantified as numerical percentages. Numerical data will be presented according to its distribution. If the data adhere to a normal distribution, they will be given as mean $\pm$ SD; conversely, if the numerical data diverge from a normal distribution, they will be represented as median (minimum–maximum). All variables were examined for disparities between two groups: HELLP syndrome or non-HELLP syndrome. Independent t-tests or Mann–Whitney U tests will be employed for continuous variables, while Chi-square or Fisher's exact tests will be used for categorical variables, as appropriate.

Results

A total of 1808 pregnant women with PE were identified, comprising 219 (12.1%) with HELLP syndrome and 1589 (87.9%) without HELLP syndrome. No disparities in maternal characteristics were observed between the two groups regarding maternal age, BMI, parity, obesity, multiple gestation, and IVF pregnancies. The HELLP syndrome group had significantly elevated systolic ($p=0.033$) and diastolic ($p<0.001$) blood pressure compared to the non-HELLP syndrome group. The HELLP syndrome group exhibited significantly elevated risk factors, including a history of chronic hypertension ($p<0.001$) and kidney disease ($p=0.012$), compared to the non-HELLP group. No differences existed between the two groups regarding abortion history, FGR, diabetes mellitus (DM), autoimmune diseases, and prior occurrences of PE. Maternal characteristics and risk factors for both groups are presented in Table 1.

We observed variations in the types of PE between the two groups regarding maternal outcomes. In the HELLP syndrome cohort, early-onset PE was prevalent (53.9%), but in the non-HELLP syndrome cohort, late-onset PE was predominant (69.7%) ($p<0.001$). Women in HELLP syndrome group had a significantly higher incidence of maternal death compared to the non-HELLP syndrome group (3.7% vs 1%, $p=0.005$). The presence of HELLP syndrome increased the risk of maternal death 3.6 fold (RR: 3.63, 95% CI: 1.57–8.38, $p=0.0025$). The HELLP syndrome group had a greater prevalence of severe complications associated with PE compared to the non-HELLP

Table 1 General maternal characteristics

General Characteristic	HELLP Syndrome (n = 219) n (%)	PE Non-HELLP Syndrome (n = 1589) n (%)	P Value	RR (95% CI)
Maternal Ages	32.25 $\pm$ 6.415	31.71 $\pm$ 7.280	-	-
≥ 35 yo	80 (36.5%)	573 (36.1%)	0.897 ^b	-
< 35 yo	139 (63.5%)	1015 (63.9%)		
BMI on admission	28.772 $\pm$ 6.225	28.711 $\pm$ 6.285	0.948 ^c	-
Systolic BP	168.84 $\pm$ 25.132	165.01 $\pm$ 20.293	0.033 ^c	-
Diastolic BP	105.17 $\pm$ 18.595	101.01 $\pm$ 14.298	< 0.001 ^c	-
Obesity	111 (50.7%)	754 (47.5%)	0.383 ^b	-
Parity				-
Nulliparity	61 (27.9%)	466 (29.4%)	0.645 ^b	-
Multiparity	158 (72.1%)	1121 (70.6%)		
IVF Pregnancy	0 (0%)	1 (0.1%)	1.000 ^a	-
Multiple Pregnancy	5 (2.3%)	61 (3.9%)	0.229 ^b	-
History of Disease				
History of Abortion	48 (21.9%)	376 (23.7%)	0.568 ^b	-
History of Low Birth Weight	32 (14.7%)	209 (13.2%)	0.539 ^b	-
Chronic Hypertension	59 (26.9%)	265 (16.7%)	< 0.001 ^b	1.62 (1.27–2.06)
Pre-gestational DM	7 (3.2%)	73 (4.6%)	0.346 ^b	-
Renal disease	6 (2.7%)	11 (0.7%)	0.012 ^a	3.96 (1.48–10.59)
Autoimmune disease	5 (2.3%)	20 (1.3%)	0.216 ^a	-
History of PE	31 (14.2%)	191 (12%)	0.370 ^b	-

^aFisher exact test

^bChi-square

^cMann-whitney

group, including eclampsia, pulmonary edema, acute renal failure, hypertensive emergency, cerebrovascular accident (CVA), and intensive care unit (ICU) admission ($p < 0.001$). We didn't found any event of subcapsular liver hematoma in our series. The existence of HELLP syndrome increase the need of ICU admission of 2.2 fold (RR: 2.21, 95% CI: 1.73–2.82; $p < 0.0001$). The prevalence of (mostly iatrogenic) preterm delivery at gestational ages under 37 and under 34 weeks was significantly greater in the HELLP syndrome cohort compared to the non-HELLP cohort ($p < 0.001$). Women in the HELLP syndrome group received more MgSO₄ and corticosteroids for fetal lung maturation. We also analyzed the incidence of complications during labor in both groups. The prevalence of eclampsia and cerebrovascular accidents during labor was markedly elevated in the HELLP syndrome cohort ($p < 0.05$). HELLP syndrome elevated the risk of eclampsia by 2.3-fold (RR: 2.28, 95% CI: 1.18–4.42; $p = 0.01$) and the risk of cerebrovascular accident (CVA) by 36-fold (RR: 36.14, 95% CI: 1.74–750.28; $p = 0.002$). No differences were observed in other complications during labor, including intrapartum eclampsia, CVA, and postpartum hemorrhage. Maternal outcomes, management, and labor complications in both cohorts are presented in Table 2. The laboratory results indicated that the cohort

of women with HELLP syndrome exhibited considerably poorer values compared to the cohort of mothers with non-HELLP PE. In the HELLP syndrome group, there were decreased levels of platelets and serum albumin, and elevated levels of ALT, AST, BUN, SC, leukocytes, and urine protein, compared to the non-HELLP group ($p < 0.05$).

The HELLP syndrome cohort experienced markedly poorer perinatal outcomes across all parameters as compared to the non-HELLP syndrome cohort. Women in the HELLP syndrome cohort experienced premature deliveries, reduced fetal biometry, FGR, and an increased incidence of major neonatal morbidities. The neonatal death rate and intrauterine fetal demise (IUFD) in the HELLP cohort were markedly elevated compared to the non-HELLP cohort ($p < 0.001$). HELLP syndrome elevated the risk of neonatal mortality by 1.8-fold (RR: 1.85, 95% CI: 1.22–2.81, $p = 0.003$) and the risk of intrauterine fetal demise (IUFD) by 2.6-fold (RR: 2.66, 95% CI: 1.73–4.07, $p < 0.0001$). Infants born to women with HELLP syndrome had a higher likelihood of NICU admission and encountered problems such as sepsis and respiratory distress syndrome compared to those in the non-HELLP syndrome group ($p < 0.001$). A summary of perinatal outcomes can be seen in Table 3.

Table 2 Maternal outcomes, management and labor complications

Maternal Outcomes	HELLP Syndrome (n = 219) n (%)	PE Non-HELLP Syndrome (n = 1589) n (%)	P Value	RR (95% CI)
Onset PE				
Early-onset PE	118 (53.9%)	482 (30.3%)	< 0.001 ^b	1.78 (1.54–2.05)
Late-onset PE	101 (46.1%)	1107 (69.7%)		
Eclampsia	39 (17.8%)	97 (6.1%)	< 0.001 ^b	2.92 (2.07–4.11)
Pulmonary edema	24 (11%)	78 (4.9%)	< 0.001 ^b	2.23 (1.44–3.45)
Acute Kidney Injury	23 (10.5%)	30 (1.9%)	< 0.001 ^b	5.56 (3.29–9.40)
Emergency Hypertension (> 180/110 mmHg)	76 (34.7%)	331 (20.8%)	< 0.001 ^b	1.67 (1.36–2.05)
CVA	4 (1.8%)	1 (0.1%)	< 0.001 ^a	29.02 (3.26–258.49)
Preterm birth < 37 weeks	127 (58%)	656 (41.3%)	< 0.001 ^b	1.40 (1.24–1.60)
Preterm birth < 34 weeks	118 (53.9%)	446 (28.1%)	< 0.001 ^b	1.92 (1.66–2.22)
ICU Admission	63 (28.8%)	207 (13%)	< 0.001 ^b	2.21, (1.73–2.82)
Maternal Death	8 (3.7%)	16 (1%)	0.005 ^a	3.63 (1.57–8.38)
Management				
Aspirin during ANC	10 (4.6%)	69 (4.4%)	0.906 ^b	-
MgSO ₄	202 (95.3%)	1345 (86.7%)	< 0.001 ^b	1.09 (1.04–1.14)
Steroid for fetal lung maturation	106 (52.2%)	574 (37.8%)	< 0.001 ^b	1.34 (1.15–1.56)
Mode of Delivery				
Vaginal	28 (12.8%)	245 (15.7%)	0.276 ^b	-
Cesarean Section	190 (87.2%)	1317 (84.3%)		
Labor Complications				
Intrapartum eclampsia	11 (5%)	35 (2.2%)	0.013 ^b	2.28 (1.18–4.42)
CVA intrapartum	2 (0.9%)	0 (0%)	0.015 ^a	36.14 (1.74–750.28)
PPH	5 (2.3%)	30 (1.9%)	0.605 ^a	-

^aFisher exact test

^bChi-square

Table 3 Perinatal outcomes

Perinatal Outcomes	HELLP Syndrome (n = 219) n (%)	PE Non-HELLP Syndrome (n = 1589) n (%)	P Value	RR (95% CI)
GA on delivery	32.74 ± 4.182	34.64 ± 3.985	< 0.001 ^c	-
Fetal Birth-weight (gram)	1859.89 ± 796.915	2302.02 ± 866.288	< 0.001 ^c	-
Birthweight centile	36 ± 32.8	41 ± 33.4	0.016 ^c	-
Birthweight centile < 10%	n (%)			
Birthweight centile < 5%				
Fetal height (cm)	40.89 ± 9.169	43.43 ± 6.691	< 0.001 ^c	-
FGR	50 (22.8%)	252 (15.9%)	0.010 ^b	1.44 (1.1–1.88)
Intra Uterine Fetal Death (IUFD)	26 (11.9%)	71 (4.5%)	< 0.001 ^b	2.66 (1.73–4.07)
Apgar score 1st minutes				
≥ 7	64 (29.2%)	862 (54.2%)	< 0.001 ^b	1.54 (1.4–1.71)
< 7	155 (70.8%)	727 (45.8%)		
Apgar score 5th minutes				
≥ 7	125 (57.1%)	1269 (79.9%)	< 0.001 ^b	2.13 (1.78–2.56)
< 7	94 (42.9%)	320 (20.1%)		
NICU Admission	81 (37.7%)	330 (21.6%)	< 0.001 ^b	1.78 (1.46–2.17)
Respiratory distress syndrome (RDS)	53 (24.9%)	201 (13.1%)	< 0.001 ^b	1.91 (1.46–2.5)
Intracranial Haemorrhage (ICH)	1 (0.5%)	2 (0.1%)	0.323 ^a	-
Necrotizing Enterocolitis (NEC)	2 (0.9%)	17 (1.1%)	1.000 ^a	-
Neonatal sepsis	26 (12.2%)	52 (3.4%)	< 0.001 ^b	3.63 (2.32–5.68)
Neonatal death	25 (11.6%)	98 (6.4%)	0.005 ^b	1.85 (1.22–2.81)

^aFisher exact test^bChi-square^cMann-whitney

A logistic regression analysis was conducted to evaluate maternal-perinatal outcomes significantly influenced by HELLP syndrome. Eclampsia, AKI, hypertensive emergency, preterm birth before 37 weeks, preterm birth before 34 weeks, IUFD, and neonatal sepsis were substantially correlated with the occurrence of HELLP syndrome. Table 4 and Fig. 1 presents a summary of the

Table 4 Logistic regression of maternal and perinatal outcomes based on HELLP syndrome

Maternal Outcomes	p values	aOR (95% CI)	Perinatal Outcomes	p value	aOR (95% CI)
Eclampsia	< 0.001	2.50 (1.50–4.18)	FGR	0.917	1.02 (0.68–1.53)
Pulmonary edema	0.513	1.21 (0.68–2.14)	IUFD	0.01	2.18 (1.21–3.95)
AKI	< 0.01	4.11 (2.07–8.15)	NICU admission	0.056	1.47 (0.99–2.19)
Emergency Hypertension	0.048	1.42 (1.01–2.01)	RDS	0.799	0.94 (0.58–1.52)
CVA	0.250	6.53 (0.27–160.35)	Neonatal sepsis	0.011	2.32 (1.21–4.42)
Preterm birth < 37 weeks	0.013	1.54 (1.10–2.17)	Neonatal death	0.077	0.59 (0.33–1.06)
Preterm birth < 34 weeks	< 0.001	1.80 (1.28–2.53)			
ICU Admission	0.112	1.39 (0.93–2.08)			
Maternal death	0.325	1.75 (0.58–5.31)			
Eclampsia intrapartum	0.317	0.63 (0.25–1.57)			
CVA intrapartum	0.999	-			

logistic regression analysis on pregnancy outcomes in HELLP syndrome.

Discussion

This Indonesian study based on data from 30 major hospitals revealed that the presence of HELLP syndrome significantly increase risk of maternal and perinatal mortality and morbidity in PE pregnancies. The likelihood of maternal death escalates by 3.63 times, whereas the probability of neonatal death rises by 1.85 times in pregnant women diagnosed with HELLP syndrome compared with non-HELLP PE patients. This finding aligns with the research conducted by Lisonkova S et al., which identified a tenfold increase in the risk of maternal death and a 4.5-fold increase in perinatal death among pregnant women diagnosed with HELLP syndrome [16]. In the meantime, a study conducted by Anitha GS et al. reported a prevalence of maternal death at 7.14% and perinatal death at 46.43% in pregnancies affected by HELLP syndrome [7].

The presence of HELLP syndrome also significantly increased risk of other major PE complications such as pulmonary edema, acute kidney injury (AKI), eclampsia, CVA and emergency hypertension. Many studies has shown that HELLP syndrome has been associated with AKI [17, 18]. This study found that the incidence of AKI among individuals with HELLP syndrome was 10.5%. This figure is relatively low when compared with other studies that reported the incidence of acute kidney injury

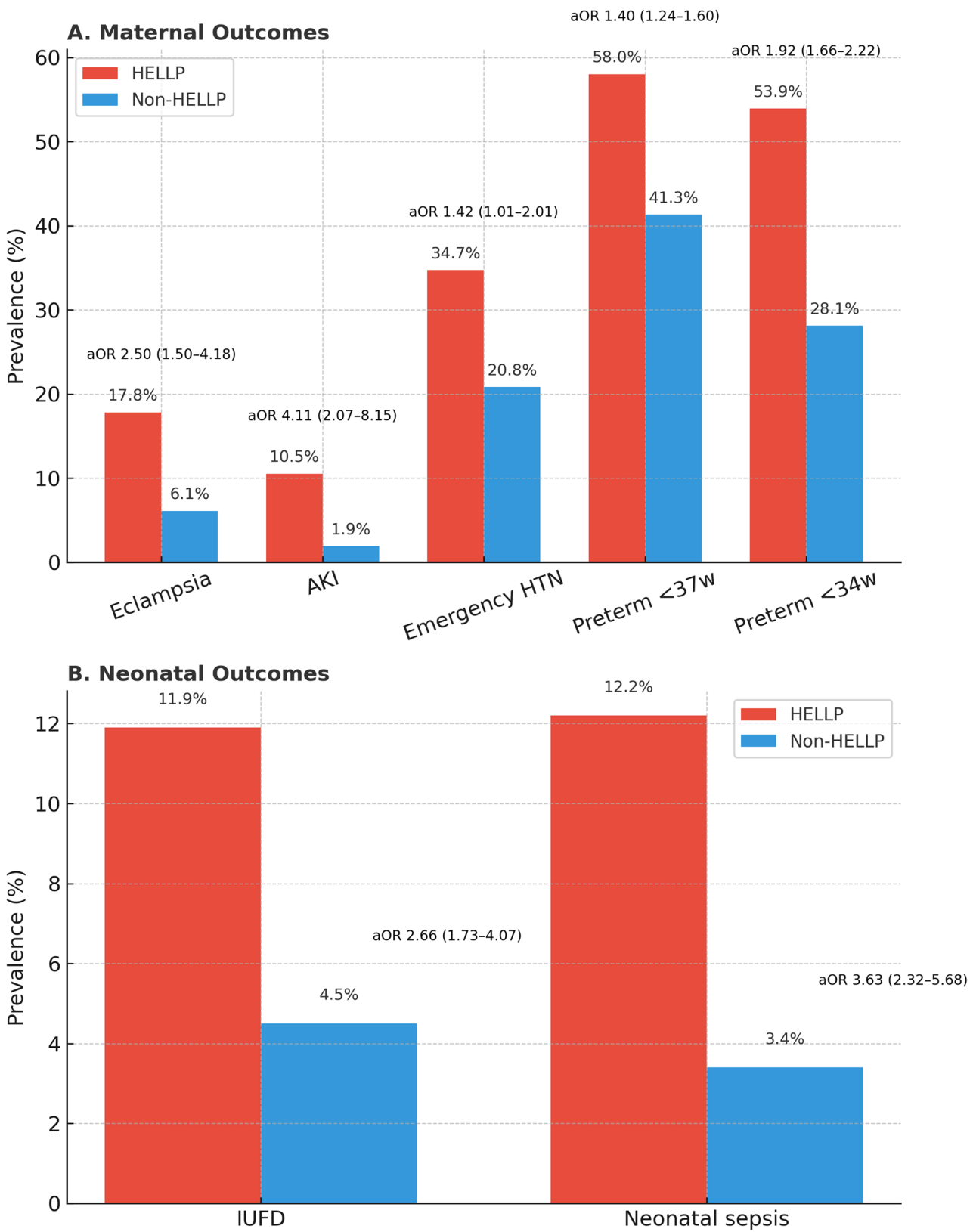


Fig. 1 Maternal and neonatal outcomes in preeclamptic women with and without HELLP syndrome. Panel A shows maternal complications, and Panel B shows neonatal outcomes. Bars indicate prevalence (%) in each group, with adjusted odds ratios (aOR, 95% CI) displayed above. HELLP syndrome is associated with significantly higher maternal and neonatal morbidity

in women with HELLP syndrome to be between 7–60% [19, 20]. Indeed, HELLP syndrome and PE are among the predominant etiologies of AKI during pregnancy, among acute fatty liver of pregnancy, thrombotic microangiopathies, sepsis, and postpartum hemorrhage (PPH) [17]. Acute kidney injury in the context of HELLP syndrome and PE has been linked to placental abruption and pulmonary edema [11]. Regrettably, this study lacks data regarding the incidence of placental abruption. Numerous studies have shown that acute kidney injury (AKI) is a risk factor for maternal mortality in patients with HELLP syndrome [11, 21].

Moreover, HELLP syndrome markedly elevated the risk of CVA and eclampsia during childbirth. Women diagnosed with PE exhibit an elevated risk of both ischemic and hemorrhagic strokes. Approximately 36% of women experiencing pregnancy-associated strokes (PASs) also have comorbid PE [22]. PE elevates the risk of stroke during the puerperium by as much as six times [23]. Elevated severity of PE, encompassing HELLP syndrome, correlates with a higher likelihood of cerebrovascular events. A retrospective research in Japan determined that PE (11.7%) and HELLP syndrome (8.1%) are the primary causes of cerebrovascular accidents and hemorrhagic strokes [24].

HELLP syndrome represents an advanced stage of PE. As such this large data set also highlights the ongoing problems with early detection and management of PE in Indonesia. With adequate management of PE in the early stage, the occurrence of HELLP syndrome in the majority of these PE pregnancies could have been prevented [25]. Particularly PE patients with very high sFlt1/PLGF ratios are at risk of major PE complications. In a comparison involving 125 women with PE without severe features, it was observed that 25 women with PE exhibiting any of the following conditions: HELLP syndrome, disseminated intravascular coagulation, or severe renal involvement, demonstrated sFlt-1 levels that were 2.63-fold higher. Additionally, sFlt-1/PIGF levels were found to be 10.07-fold higher, while PIGF levels were 74% lower [26].

From a clinical management point of view, women in HELLP syndrome received Magnesium sulphate (part of national guidelines) and corticosteroid therapy more frequently than the non-HELLP group. A subset of the non-HELLP cohort (13.3%) did not receive MgSO₄ due to the lack of severe PE symptoms or sequelae. Magnesium sulfate is indicated solely for cases of PE with severe features. In the HELLP cohort, 4.7% of cases did not receive MgSO₄ treatment. The retrospective nature of the study results in a lack of comprehensive data on this matter. However, this trial was confined to a referral hospital, where patients often arrived in active labor that progressed rapidly, preventing the administration of MgSO₄. Furthermore, in some cases, HELLP symptoms

were only partially present, leading to an ambiguous diagnosis; therefore, MgSO₄ was not administered. Corticosteroids, although controversial are also commonly used in Indonesia in an attempt to improve maternal outcome [2, 27]. Corticosteroid administration has been shown to improve platelet count, serum level of ALT, AST, LDH and reduces hospital/ICU stay. However corticosteroid use did not show any benefit in maternal and fetal overall mortality [28]. This is also supported with the study from Ernawati et al. in Surabaya tertiary care hospital. In fact the administration of steroid might be associated with higher risk of maternal infection [27]. The study revealed minimal utilization of aspirin for preeclampsia prophylaxis in both cohorts (<5%). This circumstance directly contributes to elevated rates of preeclampsia and severe preeclampsia (HELLP syndrome). The inadequate coverage of preeclampsia prophylaxis with aspirin represents a global issue, affecting both low- and middle-income countries (LMICs) and high-income countries (HICs) [29]. Retrospective studies conducted in the United States and England indicate that merely 30% of pregnant women identified as high risk for preeclampsia through screening are prescribed aspirin [30, 31]. Consequently, it is evident that aspirin coverage in low- and middle-income countries is significantly lower. This data may indicate a potential reduction in the incidence of preeclampsia and severe preeclampsia in Indonesia. Enhancing aspirin accessibility may serve as a crucial national initiative to decrease the prevalence of preeclampsia and its associated severe complications in Indonesia. Although HELLP syndrome is not in itself an indication for cesarean section, the majority of the cases in both HELLP and non-HELLP PE patients were delivered by caesarean section. The presence of comorbidities before or during labor such as eclampsia, cerebrovascular accident, pulmonary edema, AKI, or hypertensive emergencies may necessitate expedited delivery, potentially via cesarean section [32, 33].

With regards to perinatal outcomes, our study found that HELLP syndrome is associated with higher risk of adverse outcomes. Neonates born to mothers with HELLP syndrome had significantly lower birth weight and higher risk of being born premature, with lower 1 and 5 min Apgar scores, NICU admission, neonatal morbidity and mortality. These findings are consistent with previous studies indicating the negative impact of HELLP syndrome on fetal outcomes, particularly those related to prematurity and asphyxia [8]. Adverse neonatal outcomes in the HELLP syndrome cohort were correlated with gestational age at delivery. The HELLP syndrome group had a markedly greater incidence of preterm delivery in comparison to the non-HELLP cohort [12].

Conclusion

This study confirms that HELLP syndrome significantly increases maternal and neonatal morbidity and mortality in preeclampsia cases, with higher risks of severe complications such as pulmonary edema, acute kidney injury, eclampsia, and cerebrovascular accidents. It is also linked to preterm birth, NICU admission, stillbirth and neonatal mortality. These findings highlight the need for improved early detection and management of preeclampsia through better antenatal screening, close monitoring, and timely interventions. Strengthening critical care and neonatal support, especially in low-resource settings, could help reduce adverse outcomes. Further research is needed to develop effective strategies for early prediction and prevention.

Abbreviations

AKI	Acute kidney injury
ALT	Alanine aminotransferase
ANC	Antenatal care
AST	Aspartate aminotransferase
BMI	Body mass index
BUN	Blood Urea Nitrogen (BUN)
CVA	Cerebrovascular accident
DBP	Diastolic blood pressure
DM	Diabetes mellitus
FGR	Fetal growth restriction
GA	Gestational age
HELLP	Hemolysis, elevated liver enzymes, and low platelet count
ICH	Intracranial hemorrhage
ICU	Intensive care unit
IUFD	Intra-uterine fetal demise
IVF	In vitro fertilization
LDH	Lactate dehydrogenase
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
PASs	Pregnancy-associated strokes
PE	Preeclampsia
PPH	Postpartum hemorrhage
RDS	Respiratory distress syndrome
SBP	Systolic blood pressure
SC	Serum creatinine

Acknowledgements

We express our gratitude to all members of the HFKM Preeclampsia Research Group who contributed to the successful completion of this study: Muhammad Ilham Aldika Akbar, Khanizyah Erza Gumilar, Rozi Aditya Aryanandha, Adhi Pribadi, Muhammad Alamsyah Aziz, Ernawati, Manggala Pasca Wardhana, Agus Sulistyono, Muhammad Adrianes Bachnas, Rima Irwinda, Bambang Rahardjo, Aditiawarman, Agus Rusdhy Hariawan Hamid, Julian Dewantiningrum, Fransiscus Octavianus Hari Prasetyadi, Febriansyah Darus, Ariawan Ditya B, Jonathan Kevin Djuanda, Ruth Widhiati Raharjo Putri, Tedy Teguh Satriadi, Alini Hafiz, Roza Sriyanti, A.I Suratman, Aryani Aziz, Novi Resistantie, Ario Danianto, Yuyun Lisnawati, Sri Pudyastuti, Besari Adi Pramono, Dharma Putra P Banjarnahor, Dhanny Primatara Johari Santoso, Defrin, Junneke J Kaeng, Nutria Widya Purna Anggraini, Anak Agung Gede Putra Wiradyana, Anak Agung Ngurah Jaya Kusuma, Nuswil Bernolian, Joserizal Serudji, Cut Meurah Yeni, Maisuri T Chalid, Yusrawati, John J.E. Wantania, Sarma Lumbanraja, Sri Sulistyowati, Noroyono Wibowo, Johannes C Mose, Erry Gumilar Dachlan, Gustaaf Dekker.

Authors' contributions

EE conceived the study, designed the methodology, supervised data analysis, writing the initial draft and revised the final draft. MIAA conceived the study, designed the methodology, supervised data analysis, statistical analysis, and revised the final draft. RAA, MAB, RI, JD, NB, and GD contributed to study design refinement, data interpretation, and manuscript drafting. The HFKM

Preeclampsia Research Group coordinated multicenter data collection across participating hospitals. All authors critically reviewed and approved the final version of the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate

The study proposal received approval from the ethics council of Airlangga University Hospital has issued ethical approval for this research (approval no. 052/KEP/2024, protocol number UA-02–24074). This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments. The study protocol was reviewed and approved by the appropriate institutional ethics committee. Given the retrospective nature of the study and the use of anonymized medical record data only, the requirement for informed consent was waived by the ethics committee.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 19 October 2025 / Accepted: 15 December 2025

Published online: 22 December 2025

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